PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

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To:

see form PCT/ISA/220

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43*bis*.1)

Date of mailing *(day/month/year)* see form PCT/ISA/210 (second sheet)	
Applicant's or agent's file reference see form PCT/ISA/220	**FOR FURTHER ACTION** See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/NL2004/000617	03.09.2004	05.09.2003

International Patent Classification (IPC) or both national classification and IPC
G01N33/50

Applicant
NEDERLANDSE ORGANISATIE VOOR TOEGEPAST NATUURW...

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☒ Box No. VII Certain defects in the International application
- ☐ Box No. VIII Certain observations on the International application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:

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WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/NL2004/000617

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☐ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☐ in written format

   ☐ in computer readable form

   c. time of filing/furnishing:

   ☐ contained in the international application as filed.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 17-20 [full]

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination *(specify)*:

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the whole application or for said claims Nos. 17-20 [full]

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form ☐ has not been furnished

☐ does not comply with the standard

the computer readable form ☐ has not been furnished

☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-16
	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-16
Industrial applicability (IA)	Yes:	Claims	1-16
	No:	Claims	

2. Citations and explanations

see separate sheet

Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1 The following documents (D1-D2) are referred to in this communication; the numbering will be adhered to in the rest of the procedure:

D1: US 2003/096309 A1 (STOCKWELL BRENT R ET AL) 22 May 2003 (2003-05-22)

D2: WO 03/017177 A (BEYONG GENOMICS INC) 27 February 2003 (2003-02-27)

2 NOVELTY

2.1 The subject-matter of claims 1-16 is considered new in the sense of Article 33(2) PCT.

3 INVENTIVE STEP

3.1 The present application does not meet the requirements of Article 33(1) PCT, because the subject-matter of claims 1-16 does not involve an inventive step in the sense of Article 33(3) PCT.

3.1.1 The subject-matter of claim 1 is not considered inventive under Article 33(3) PCT. Here, D1 is considered the closest prior art. This document discloses (the references in parentheses applying to this document): a method for determining the impact of synthetic drug combinations on a disease state comprising the steps of: (a) determining a biological profile of the disease by comparing the biological profile of a group with symptoms of the disease with the biological profile of a reference group using a multivariate analysis (in this case, the disease profile is TNFalpha secretion (example 4)); (b) obtaining a set of drugs that are effective against a particular disease profile (paragraph [0020-0021]; (c) preparing a set of multicomponent product mixtures that are expected to display

an impact on the disease profile (table 2); (d) determining the impact of the multicomponent product mixtures on the biological profile of the disease using multivariate analysis (in this case, the effect of different concentrations of amoxapine and prednisolone on the disease profile is determined (table 2)).

3.1.2 The additional technical feature of claim 1 over D1 is that step (b) involves identifying input drugs (compositions) that are effective against a particular disease by a screening process rather than selecting drugs that are already known to be effective against a particular disease (i.e. have already been screened by someone in the past).

3.1.3 The problem to be solved by the present invention may therefore be regarded as a further method for identifying drug-drug interactions.

3.1.4 The solution to this problem is to use input drugs that are identified as effective against a particular disease by an actual screening process rather than using input drugs that are already established as effective against a particular disease.

3.1.5 The solution to the problem merely involves adding unnecessary steps to the method of D1. The skilled person knows that the test drugs used in D1 have at some point been subjected to a screening process in the past similar to that of claim 1. Thus, in D1, the skilled person saves himself work by using products that are already known to display an impact on the biological profile of the disease, rather than undertaking this work himself. As such, it would be obvious to provide an alternative method to that of D1, according to claim 1, by adding a step to the method of D1 that is unnecessary and that would have been undertaken by someone else prior to the start of the method of D1. Therefore the subject-matter of claim 1 does not involve an inventive step in the sense of Article 33(3) PCT.

3.2 The subject-matter of dependent claims 2-16 merely adds routine modification

options to the subject-matter of claim 1 and is therefore obvious to a person skilled in the art. For this reason, the subject-matter of the said claims does not involve an inventive step in the sense of Article 33(3) PCT either. Furthermore, it should be noted that it would be obvious to incorporate the teachings of D2 concerning multivariate analysis into D1, since D2 contains a direct pointer indicating that its teachings are relevant to testing pharmaceutical compounds (claim 40).

4 INDUSTRIAL APPLICABILITY

4.1 The subject-matter of claims 1-16 is considered industrially applicable in the field of drug screening (Article 33(4) PCT).

Re Item VII
Certain defects in the international application

1 The Independent claims of the present application are not in the two-part form in accordance with Rule 6.3(b) PCT. In the present case, it is felt that it would be particularly appropriate to use the two-part form when filing amended claims that take account of the above objections, with those features known in combination from the prior art (D1) being placed in the preamble (Rule 6.3(b)(I) PCT) and with the remaining features being included in the characterising part (Rule 6.3(b)(ii) PCT).